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Evaluation of eight cases of confirmed *Bordetella bronchiseptica* infection and colonization over a 15-year period

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Abstract

We describe eight human cases of *Bordetella bronchiseptica* infection and colonization over a 15-year period. Amongst the eight patients, seven had significant underlying disease. Cat exposure was documented in three cases. Symptoms ranged from asymptomatic carriage to severe pneumonia. We could not identify a homogeneous pattern of clinical disease among symptomatic patients. Although *B. bronchiseptica* infection remains a rare clinical condition among humans, it should be considered as potentially pathogenic when found in airways of immunocompromised patients.

Keywords: *Bordetella bronchiseptica*, case series, clinical study, epidemiology, humans, outcome, Switzerland

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Bordetella spp. are aerobic coccobacilli known to be present in the upper respiratory tract of many animals [1]. *B. bronchiseptica* infections are uncommon in humans [2]. The literature on this subject is subsequently poor. Two comprehensive reviews have been published in the last two decades. The first included 25 cases from 1911 to 1990 [1]. However, the presence of *B. bronchiseptica* was microbiologically confirmed in only ten patients. The other study, published in 1995, included 52 patients but no details were provided about the microbiological identification of *B. bronchiseptica* [3]. Another study published in 2005 focused on the pathogenesis but gave little information on human infections [4]. Recently, several case reports addressed the problem in cystic fibrosis patients [5], HIV patients [2,6] or children with lung transplants [7]. Facing this lack of recent information, we decided to review all cases detected at our institution from 1993 to 2008.

The present study was undertaken at the Geneva University Hospitals, a 2220-bed tertiary care centre. We performed a retrospective case review approved by the institutional ethics review board and based on computerized laboratory log files, examining the pattern of disease caused by *B. bronchiseptica*, addressing underlying conditions and exposures, and examining antimicrobial treatment in relation to patient outcome. To avoid misclassification bias, we included only patients with verified *B. bronchiseptica* isolates because automated identification systems can lead to misclassification as *Acinetobacter* spp. or other nonfermentative Gram-negative rods. Most cases were first identified by API 20NE gallery or VITEK2 (bioMerieux SA, Marcy-l'Etoile, France) phenotypic identification systems, and then supported by a positive oxidase reaction. All available stored

isolates (4/8) were verified as *B. bronchiseptica* by 16s rDNA sequencing and a positive oxidase reaction, confirming that our phenotypic identification was reliable. Because the method of previous antimicrobial susceptibility testing (AST) could not be verified in this retrospective study, we performed new AST [MIC using the E-test (AB Biodisk, Solna, Sweden)] on all available isolates, despite the absence of CSLI guidelines for the E-test AST of *B. bronchiseptica* [8]. Therefore, *E*-tests were performed as previously recommended [9]. Considering the fastidious character of the microorganism, a second MIC determination was performed at 48 h, but this did not reveal any relevant change in AST.

During a 15-year period, eight patients had confirmed *B. bronchiseptica* infection (n = 3), co-infection (n = 2) or colonization (n = 3). Table 1 summarizes the key features of these cases. All specimens except one were retrieved from the airways. Cases were equally distributed among gender and age groups. Amongst the eight patients, seven had significant underlying disease, including four patients with severe lung disease, two patients with AIDS and one patient with autoimmune neutropenia. Three patients had documented contact with cats prior to infection. In one case, the cat itself had respiratory symptoms.

The disease pattern related to *B. bronchiseptica* was not uniform. Except for one chronic obstructive pulmonary disease (COPD) patient who presented with colitis and septic shock unrelated to *B. bronchiseptica* airway colonization, three clinical presentations were observed: (i) two patients were asymptomatic carriers of *B. bronchiseptica*; (ii) two patients had symptoms of bronchitis; and (iii) three patients presented with severe pneumonia. In two of these latter cases, the pathogenic role of *B. bronchiseptica* was established (e.g. lung abscess). The remaining patient with pneumonia was co-infected with *Pneumocystis jiroveci*.

All available isolates (n = 4) were susceptible to amoxicillin-clavulanate, piperacilin-tazobactam, imipenem, amikacin, gentamicin, tobramycin, ciprofloxacin, and tigecyclin. Trimethoprim-sulfamethoxazole was susceptible in two of four cases only and all four isolates were resistant to erythromycin. Patients received various antibiotic treatment regimens (Table 1). In two patients with pneumonia and one patient with bronchitis, microbiological persistence of *B. bronchiseptica* was documented despite antimicrobial treatment.

Despite the inherent limitations of the retrospective design of the present study and its small sample size, several features emerge from this series of eight human *B. bronchiseptica* cases, which is one of the most comprehensive in the recent literature. Although we retrieved three cases in 2008, the overall small number of cases does not enable us to conclude an increasing incidence of human *B. bronchiseptica* cases

TABLE 1. Characteristics of patients

	Age, sex	Underlying disease	Diagnosis	Specimen	Other microorganisms	Year	Method of identification	Pathogenic role of *Bordetella bronchiseptica*	Animal exposure	Antimicrobial treatment	Short-term outcome
1	65, F	Severe COPD	Colitis with septic shock	Tracheal aspirate	*Enterobacter aerogenes*	2009	Vitek2 (99%)[a] and MALDI-TOF MS	Colonizer	Unknown	Imipenem	Death, unrelated cause
2	34, F	None	Asymptomatic	Cervical smear	None	2008	Vitek2 (99%) and oxidase	Colonizer	Cat	Amoxicilin-clavulanate	Cured
3	65, M	Peripheral neutropenia	Pneumonia with abscess	Sputum	None	2008	Vitek2 (99%) and oxidase	Infectious agent	Cat	Imipenem	Cured
4	21, M	Cystic fibrosis	Asymptomatic	Sputum	*Pseudomonas aeruginosa*	2008	Vitek2 (99%) and oxidase	Colonizer	Unknown	Trimethoprim-sulfamethoxazole and azithromycin	Cured
5	17, M	Cystic fibrosis	Bronchitis	Throat swab	β-hemolytic streptococcus group G	2006	16s rDNA sequencing and oxidase	Infectious agent	Cat[b]	Ciprofloxacin (S)[c] and tobramycin (S)	Cured
6	42, F	AIDS	Pneumonia	Broncho-alveolar lavage	*Pneumocystis jiroveci*	2001	16s rDNA sequencing and oxidase	Co-pathogen	Unknown	Trimethoprim-sulfamethoxazole (S)	Cured
7	68, M	Severe COPD	Pneumonia	Broncho-alveolar lavage	None	1999	16s rDNA sequencing and oxidase	Infectious agent	Unknown	Amoxicilin-clavulanate (S)	Cured
8	35, M	AIDS	Bronchitis	Broncho-alveolar lavage	*Pneumocystis jirovici*	1993	16s rDNA sequencing and oxidase	Co-pathogen	Unknown	No data available	Cured

[a]Vitek2 (99%): 99% refers to the probability to accurately identify the organism.
[b]In this case, the cat was reported to be coughing at the time of diagnosis.
[c]S indicates that the *B. bronchiseptica* isolate was sensible to this antibiotic according to antimicrobial susceptibility testing performed with *E*-test methodology.
COPD, chronic obstructive pulmonary disease; MALDI-TOF MS, matrix-assisted laser-desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Leipzig, Germany).

because of possible random variation. The majority of our patients presented with a significant underlying disease, mainly COPD or AIDS. The only patient without an underlying condition presented an unusual location not previously described: *B. bronchiseptica* was identified on the maternal side of the placenta of an asymptomatic woman who was admitted for delivery by Caesarean section. A laboratory contamination could be reasonably excluded.

Our analysis confirms the tropism of *B. bronchiseptica* for the respiratory tract, leading to occasional upper airway colonization, as previously described [3]. The only case of death observed was not caused by *B. bronchiseptica* because the patient was diagnosed with septic shock due to colitis.

Immunocompromised patients who own cats should be aware of this small but non-negligible threat of airway contamination with *B. bronchiseptica*. Although an animal vaccine for *B. bronchiseptica* exists [10], its efficacy remains controversial [4] and thus the vaccination of pets might not confer protection. Because of cross immunity, immunocompromised patients might, however, benefit from *B. pertusssis* vaccination, as shown in a mouse model [11].

Different antibiotic regimens were administered to our patients. This variety reflects the absence of reliable treatment recommendations. As a consequence, we cannot provide any firm conclusion on the optimal therapeutic approach. However, *B. bronchiseptica* are usually susceptible to anti-pseudomonal penicillins, carbapenems, flouroquinolones and aminoglycosides, but not to erythromycin, in contrast to other *Bordetella* species.

In summary, it remains difficult to clearly establish the pathogenic role of *B. bronchiseptica* in human disease as a result of the rare occurrence and challenging microbiological diagnosis. In the present study, we could reasonably establish the microbiological identification and pathogenic role of *B. bronchiseptica* and therefore explore its related clinical symptoms. On the basis of these cases, *B. bronchiseptica* should be considered as potentially pathogenic when found in the lower airways of immunocompromised patients.

Transparency Declaration

The authors declare that there are no conflicts of interest.

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